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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040303

Application Number: 09/138,735
Filing Date: August 24, 1998
Appellant(s): PARANHOS-BACCALA ET AL.

Mealy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 20, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because Appellants have merely pointed out differences in what the claims cover, and is not an argument as to why the claims are separately patentable. (See 37 CFR 1.192).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,302,527	Birkett et al	4-1994

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A. The rejection of claims 5, 7, 8, 10-26, 32, 34, and 36-42 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it most nearly connected, to make and/or use the invention.

The claims are directed to probes for identifying Trypanosoma cruzi, consisting essentially of a sequence having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1 or the corresponding RNA sequence, wherein said probe contains at least 5 and no more than 100 nucleotides.

The specification states that substitutions, additions or deletions may be made to the defined sequences, however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to its ability to function as a probe or primer. Further, it is unpredictable as to which nucleotides could be removed and which could be added.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the

invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. *Enzo Biochem. Inc. v. Calgene Inc.* 188 F.3d 1362, 1371, 52 USPQ2d, 1129, 1135 (Fed. Cir. 1999).

Nucleic acids consist of 4 distinct nucleotides which bind in pairs of adenine (A) = thymine (T) and guanine (G) ≡ cytosine (C). Changing any one of these nucleotides (as permitted by 85% homology) directly effects the binding activity of the probe, this results in a probe/primer which will now bind to other molecules of unknown function and unknown origin. The unpredictability of randomly altering nucleotides creates uncertainty as to what DNA molecules will now hybridize to the probe. For instance, given that there are 4 nucleotides contained with DNA, and Appellants probes can be as short as 5 nucleotides, every $(4)^5$ or 1 in 1024 nucleotides will contain an exact 5 nucleotide match. This number grows logarithmically larger when factoring in the 85% homology limitations. Given that the human genome has approximately 2,900,000,000 nucleotides, Appellants probes will be hybridizing to multiple segments of many diverse DNA molecules. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19, 24 (CCPA 1970).

Furthermore, Appellants specification does not provide any working examples of DNA probes/primers having 85% identity to SEQ ID NO: 1 or as short as 5 nucleotides.

Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art would be forced into excessive experimentation to make or use the broadly claimed invention.

B. The rejection of claims 5, 7, 8, 10-27, 32, 34, and 36-42 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, a written description rejection.

The claims are directed to probes for identifying Trypanosoma cruzi, consisting essentially of a sequence having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1 or the corresponding RNA sequence, wherein said probe contains at least 5 and no more than 100 nucleotides.

Appellants solely described activity for the described fragments is that of a probe or primer. However each of these uses is dependent upon the precise "consisting of" structure being used. Substitutions upstream, downstream, or within the recited probe will have a profound effect upon the activity of the primer or probe. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted.

Although the specification states that these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Appellant was not in possession of the claimed genus.

C. The rejection of claims 5, 8, 10-11, 17, 25-26, 32, and 39-40 rejected under 35 U.S.C. 102(b) as being anticipated by Birkett et al.

The claims are directed to probes for identifying Trypanosoma cruzi, consisting essentially of a sequence having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1 or the corresponding RNA sequence, wherein said probe contains at least 5 and no more than 100 nucleotides.

Birkett et al (US Patent Number 5,302,527) disclose of random priming with a mixed oligonucleotide kit (Multiprime Kit, Amersham). (See column 15, lines 25-30).

In view that the isolated hexamer oligonucleotide primers disclosed by Birkett et al will inherently share 85% homology with 5 consecutive nucleotides from nucleotides 1232-2207 of SEQ ID NO: 1 of the instant invention, the disclosure of Birkett et al is deemed to anticipate the claimed invention.

(11) Response to Argument

A. Appellants argue in 18 different groups. However the Examiner will address all arguments contained within the 18 different groups with a single response. Appellants argue the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Appellants further assert that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided by the claimed invention. *In re Wright* 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Appellants further assert that specifically, one of ordinary skill in the art would have been able to use these sequences as probes or primers or to generate probes and primers for the identification or amplification, respectively of Trypansoma cruzi nucleic acids. In particular it was well known in the art that nucleic acids having less than 100% homology with the complement of the target can be used as a probe or primer. Appellants assert that although the use of lower stringency conditions may increase the likelihood that the sequence binds to other molecules of unknown function and unknown origin, one of ordinary skill in the art can employ the use of additional probes and/or other techniques to confirm the identity of the identified or amplified sequence.

RESPONSE:

First, the initial burden to establish a reasonable basis to question the enablement of the claimed invention has been addressed. Nucleic acids consist of 4 distinct nucleotides which bind in pairs of adenine (A) = thymine (T) and guanine (G) ≡

cytosine (C). Changing any one of these nucleotides (as permitted by 85% homology) directly effects the binding activity of the probe, this results in a probe/primer which will now bind to other molecules of unknown function and unknown origin.

Second, Appellants further assert that specifically, one of ordinary skill in the art would have been able to use these sequences as probes or primers or to generate probes and primers for the identification or amplification, respectively of Trypansoma cruzi nucleic acids. However, while every conceivable sequence of nucleotides has the capability to function as a probe, Appellants specification provides no guidance as to which sections of the DNA molecule can be freely substituted and retain useful function for identifying Trypansoma without cross hybridizing with other homologous DNA sections of unrelated organisms. Without such guidance one of skill in the art would be left to manufacture a large number of primers, and then further determine which of this multitude retain useful binding to Trypansoma without binding so many other segments of unrelated DNA as to offer no meaningful results.

Finally, Appellants assert that although the use of lower stringency conditions may increase the likelihood that the sequence binds to other molecules of unknown function and unknown origin, one of ordinary skill in the art can employ the use of additional probes and/or other techniques to confirm the identity of the identified or amplified sequence. However, this again illustrates the Examiners point. No guidance has been provided as to which specific sequences are useful in the first place. Appellants specification merely asserts that any 5 consecutive nucleotides which share 85% homology with the disclosed sequence can function as a probe. However,

Appellants specification does not offer a single working example in this range, nor does it identify specific regions of the reference sequence that can be employed. This lack of guidance combined with nucleotide substitutions within the primer generates unpredictable results of which molecules will now hybridize to this altered nucleotide molecule. Conseqeuntly, given the lack of guidance, lack of working examples, and the unpredictable nature of substituting nucleotides within a sequence of a probe would require one of ordinary skill in the art into excessive experimentation to practice the broadly claimed invention.

B. Appellants argue in 18 different groups. However the Examiner will address all arguments contained within the 18 different groups with a single response. Appellants assert that a description is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367,370 (CCPA 1971). Appellants further assert that unlike the situation in Eli Lilly, the present specification clearly provides more than a mere statement that the claimed nucleotide sequences are part of the invention and reference to a potential method for isolating them. Instead the specification clearly indicates that the inventors isolated and sequenced SEQ ID NO: 1 and identified the portions thereof recited in claims 21-23. Appellants further assert that in addition to describing these specific sequences, the specification specifically describes nucleotide sequences having at least 85% homology with the recited sequences, particularly where each segment of 30 contiguous nucleotides of the

nucleotide sequence has at least 85% homology with a segment of 30 contiguous nucleotides of the respective portion. Appellants specifically assert that claims 10, and 24 do not recite sequences having 85% homology with the recited sequences, thus the Patent Office has not provided any basis for its determination that claims 10 & 24 are not supported by the present specification.

RESPONSE:

First, Appellants assert that unlike the situation in Eli Lilly, the present specification clearly provides more than a mere statement that the claimed nucleotide sequences are part of the invention and reference to a potential method for isolating them. However, this is precisely what Appellants have done. Appellants "description" is the identification of SEQ ID NO: 1. The written description for this molecule is not questioned. However, Appellants claims are directed to any probe having 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1, wherein said probe contains at least 5 and no more than 100 nucleotides. It is this "probe" of 85% homology and of a length of between 5 and 100 nucleotides that is being questioned. Aside from Appellants statement that the invention includes sequences of 85% homology and a length of between 5 and 100 nucleotides, no other written description has been supplied. In other words, Appellants have described a single example, and are attempting to claim a genus of claims based upon the single disclosed species.

Finally, Appellants specifically assert that claims 10, and 24 do not recite sequences having 85% homology with the recited sequences, thus the Patent Office has not provided any basis for its determination that claims 10 & 24 are not supported by the present specification. However, Appellants are respectfully directed to the claim language. Claim 10 depends upon claim 8. The limitations of claim 8, which have not gone away, allow for primers of at least 5 nucleotides, and specifically those with 5 nucleotides having 85% homology with the recited sequence. In other words primers having 5 consecutive nucleotides with at least 85% homology to SEQ ID NO: 8, 9, 10 and 12 are encompassed within the breadth of the claims. Accordingly, this claim has been properly grouped in the rejection under 35 USC 112, first, written description. Likewise, claim 24 depends upon claim 23 and includes all the limitation from claim 23. Claim 23 allows for 85% homology as well as fragments comprising 30 contiguous nucleotides. These limitations have not gone away and therefore still encompass nucleic acid fragments having 85% homology, and accordingly are appropriately grouped in the rejection under 35 USC 112, first, written description.

C. Appellants argue in 18 different groups. However the Examiner will address all arguments contained within the 18 different groups with a single response. Appellants assert that to invalidate a claim based on inherency, inherency must be a necessary result and not merely a possible result. The mere fact that a certain thing may result from a given set of circumstances is not enough. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). Appellants further assert that claim 8 does not

encompass every primer that would hybridize to any part of SEQ ID NO: 1, instead claim 8 encompasses primers having 5 to 30 nucleotides, wherein the primer consists essentially of a sequence having at least 85% homology with nucleotides 1232-2207 of SEQ ID NO: 1. Appellants further assert that Birkett does not teach any of the hexamers contains at least 5 consecutive nucleotides of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1. Appellants further assert that claim 10 further recites that the primer consists essentially of a nucleotide selected from the group consisting of SEQ ID NO: 8, 9, 10 and 12, all of which contain at least 18 nucleotides and are therefore clearly not one of the random hexamers contained in the kit described by Birkett. Appellants finally assert that Birkett et al do not teach of a capture probe and a detection probe having nucleotide sequences that are different from one another.

RESPONSE:

First, Appellants assert that to invalidate a claim based on inherency, inherency must be a necessary result and not merely a possible result. The mere fact that a certain thing may result from a given set of circumstances is not enough. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). However, the analytic tool of "inherency" allows determination of whether subject matter that is not taught in the single reference was nonetheless know in the field of the invention. This was acknowledged in *EMI Group North America, Inc. v. Cypress Semiconductor Corp.*, 268 F. 3d 1342 (60 USPQ2d 1423) (Fed. Cir. 2001). Furthermore, under the doctrine of

inherency, if an element is not expressly disclosed in a prior art reference, the reference will still be deemed to anticipate a subsequent claim if the missing element "is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Cont'l Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

Appellants further assert that Birkett does not teach any of the hexamers contains at least 5 consecutive nucleotides of a nucleotide sequence that is identical or fully complementary to a sequence starting at nucleotide 1232 and ending at nucleotide 2207 of SEQ ID NO: 1. However, those of skill in the art would clearly recognize that the random hexamer kit contains virtually every possible combination of six consecutive nucleotides that can be created. Thus, those of ordinary skill in the field of the invention would recognize that any 6 consecutive nucleotide hexamer (as well as those having 85% identity to 6 consecutive nucleotide hexamers) claimed would be anticipated by a kit that contains every possible combination of six consecutive nucleotides, even if the kit does not specifically identify the precise structure of every probe contained within the kit. Furthermore, as stated in the response mailed October 3, 2003, Appellants actually used random hexamer probes to isolate SEQ ID NO: 1 of the instant invention. (Specification page 23). Appellants have not offered any response to this observation. Since the Patent office does not have the facilities for examining and comparing Applicants product with the product of the prior art reference, the burden is on Applicants to show an unobvious distinction between the material structural and

functional characteristics of the claimed product and the product of the prior art. *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Appellants further assert that claim 10 recites that the primer consists essentially of a nucleotide selected from the group consisting of SEQ ID NO: 8, 9, 10 and 12, all of which contain at least 18 nucleotides and are therefore clearly not one of the random hexamers contained in the kit described by Birkett. However, Appellants are again respectfully directed to the claims. Claim 10 depends upon claim 8, which recites the limitations that the primer "is at least 5" nucleotides and has 85% homology to the recited sequence. Again these limitations have not disappeared. As such the claims include primers as short as 5 consecutive nucleotides and 85% identity with the recited sequences, and accordingly the disclosure of Birkett et al is deemed to anticipate these limitations.

Finally Appellants assert that Birkett et al do not teach of a capture probe and a detection probe having nucleotide sequences that are different from one another. However, Appellants are reminded that Birkett et al disclose of "random" hexamer probes, not a kit containing 4000 probes of identical structure. Accordingly each and every limitation of the claim has been addressed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Primary Examiner
March 3, 2004

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